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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/801,980	03/08/2001	Mark A. Laughlin	IN01144	5887

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SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 02/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/801,980	LAUGHLIN, MARK A.	
	Examin r	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cov r sheet with the corr spondence addr ss --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,27,28,32-36,41,42 and 44-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,27,28,32-36,41,42 and 44-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Application

1. Claims 1-49 were pending and rejected in the application in the prior action, mailed on July 15, 2003. In the Response, filed on November 17, 2003, the Applicant cancelled claims 1-24, 26, 29-31, 37-40, and 43; and amended claims 25, 28, 41.

Currently, claims 25, 27, 28, 32-36, 41, 42, and 44-49 are pending and under consideration.

Specification

2. **(Prior Objection- Withdrawn)** The disclosure was objected to for informalities on pages 3, lines 3 and 20. In view of the amendment of the specification to correct these errors, the objection is withdrawn.

Claim Objections

3. **(Prior Objection- Withdrawn)** Claims 4, 10, 19, 26, 39, and 43 were objected to in the prior action for introducing the anti-HIV therapy HAART by its acronym without first identifying the therapy by its complete title. In view of the cancellation of these claims, and the amendment of the currently pending claims to avoid this informality, the objection is withdrawn.

4. **(Prior Objection- Withdrawn)** Claim 23 was objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. In view of the cancellation of the claim, the objection is withdrawn.

5. **(New Objection)** Claim 28 is objected to for the following informalities: a period has been inserted at the end of each of subparts (b) and (c) of the claim. It is suggested that the period be replaced by a colon in subpart (b), and that the period be deleted in subpart (c).

6. **(New Objection)** Claim 41 is objected to for the following informalities: in line 5, the claim describes the administration of interferon alpha "in association with an effective amount HAART." It is suggested that the term - - of- - be inserted between the terms "effective amount" and "HAART."

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. **(Prior Rejection- Restated as necessitated by amendment and Maintained)** Claims 22 and 23 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of the cancellation of these claims, the rejection is withdrawn from these claims as moot. However, newly amended claims 25 and 28, and their dependant claims 27, and 32-36, contain similar language to that rejected in the prior action.

In particular, claim 25 restates the language of rejected claim 22, except that it now requires that the patient experience "an increase in HIV-RNA plasma levels" after the HAART treatment. In this claim, while the claim requires an increase in HIV_RNA plasma levels, it is not

clear that the levels have risen to the extent that the HIV-RNA levels are at or above those that were present prior to the HAART treatment. Clarification is required.

Claim 28 requires not only the cessation of HAART, but its re-initiation until the HIV-RNA levels are below the detectable limit, and then discontinuing the HAART and administering interferon alpha for a time sufficient to drop the level of HIV-RNA below the level present prior to HAART. In this claim, the problem is exacerbated because, at the cessation of the re-initiated HAART (which immediately precedes the interferon alpha treatment) the HIV-RNA levels are below a detectable limit-which is presumably far below the levels seen prior to the HAART treatment. It is thus unclear what is meant by this claim, because the HIV-RNA levels are already at levels below those existing prior to HAART at the time that interferon alpha is first administered. It is noted that the claimed process requires the cessation and re-initiation of HAART two times. The same lack of clarity is present in each instance.

9. **(Prior Rejection- Restated as necessitated by amendment and Maintained)** Claim 23 was rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim read on a method of promoting HIV-specific T-cell activity comprising "re-initiating administering an effective amount of an anti-HIV therapy for a time sufficient to lower HIV-RNA plasma levels below the detectable limit (50 HIV-RNA copies per mL of plasma)." It was unclear if the parenthetical was intended to define the detectable limit of HIV-RNA plasma levels below which the method must reduce the HIV-RNA levels, or if the parenthetical is identifying the level, to which the HIV-RNA is being reduced. While claim 23

has been cancelled from the application, the language which formed the basis of this rejection has been inserted into amended claim 28. Thus, the rejection is withdrawn as moot with respect to claim 23, but is extended to amended claim 28.

10. **(Prior Rejection-Withdrawn)** Claim 24 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of the cancellation of this claim, the rejection is withdrawn.

11. **(Prior Rejection- Restated as necessitated by amendment and Maintained)** Claims 25-36 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Although the rejection is withdrawn as to amended claim 25 (and dependant claim 27, and 32-36), the rejection is maintained with respect to amended claim 28, which describes several instances of promoting an HIV-1 specific T-cell activity in a patient by administering to a patient who has discontinued HAART an amount of IFN-alpha sufficient to lower the HIV-RNA plasma level below the level found prior to the initiation of HAART. It is not clear which "initiation of HAART" the phrase is referring to. I.e., it is unclear if the phrase refers to the HAART that was ceased immediately prior to the initiation of interferon alpha therapy, or if the phrase refers to the HIV-RNA levels prior to the original initiation of HAART. Clarification is required.

12. **(Prior Rejection- Withdrawn)** Claims 29 and 31were rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of the cancellation of these claims, the rejection is withdrawn.

Claim Rejections - 35 USC § 102

13. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

14. **(Prior Rejections- Withdrawn)** Claims 1, 5, and 6 were rejected in the prior action under 35 U.S.C. 102(b) as being anticipated by Testa et al. in Us Patent 5,676,942, and under 35 U.S.C. 102(a) as being anticipated by Alber et al., U.S. Patent 5,928,636. In view of the cancellation of these claims, the rejection is withdrawn.

15. **(Prior Rejection- Withdrawn)** Claims 1, 5, 6, 7, 11-17, and 41-49 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 6,277,830, issued to Ganguly et al. Claims 1, 5, 6, 7, and 11-17 have been cancelled from the application. The rejection is therefore withdrawn as moot against these claims. Claims 41-49 have been amended such that the claims now require that the patient being treated had previously discontinued HAART, and then experienced an increase in HIV-RNA levels, and have also been amended such that the anti-HIV therapy administered with the interferon alpha is HAART. Although Ganguly teaches that interferon alpha may be combined with HAART, the reference does not, as argued by Applicant, teach the

administration of such a combination to a patient who had previously discontinued HAART. The anticipation rejection is therefore also withdrawn from claims 41-49.

16. **(Prior Rejection- Withdrawn)** Claims 1-49 were rejected in the prior action under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Laughlin et al., U.S. Application Publication 2002/0182179. As indicated above, claims 1-24, 26, 29-31, 37-40, and 43 have been cancelled from the application. Pending claims 25, 27, 28, 32-36, 41, 42, and 44-49 have been amended to read on methods wherein the interferon-alpha is administered to a patient population comprising patients previously treated with HAART, and who have experienced an increase in HIV-RNA plasma levels since the discontinuation of HAART. In view of these amendments, the rejection is withdrawn as to claim 28. Further, although the Examiner considers the presently claimed methods to be obvious over teachings of the publication, because the publication does not qualify as art under 35 U.S.C. 103(c) the rejection is also withdrawn and not reformed as an obviousness rejection over claims 25, 27, 32-36, 41, 42, and 44-49.

17. **(Prior Rejection- Withdrawn)** Claims 1-49 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. These claims describe claims also described by the claims of the U.S. Application Publication 2002/0182179, naming Mark A. Laughlin (the inventor of the present application), and two others as inventors of the claimed invention. In view of the amendments to the claims, the rejection is withdrawn.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. **(New Rejection- Necessitated by Amendment)** Claims 41, 42, and 44-49 are rejected as obvious over the teachings of Ganguly et al (U.S. Patent 6,277,830, the teachings of which were described in the prior action), in view of the teachings of Davey et al. (PNAS 96(26): 15109-114), Neumann et al. (AIDS 13: 677-83), and Reynes et al. (7th Conf Retroviruses Opp Infect, abstract 542, February 17, 2000). The claims and the amendments to them have been described above. The teachings of Ganguly were described in the prior action. As indicated by the Applicant, the teachings of this patent do not suggest the use of the combination of HAART and interferon alpha in patients who have previously discontinued HAART and experienced an increase in HIV-RNA serum levels.

However, the art indicates that patients who ceased HAART were expected to suffer such HIV-RNA serum level increases. See, e.g., Davey, page 15109, left column (teaching that, after termination of HAART, there is generally a virologic relapse in the patient). Further, it was also known in the art that such relapses would not prevent the reinitiation of HAART therapy from being operative. See e.g., Neumann, abstract. Thus, from the teachings of the Davey and Neumann, it would have been obvious to those in the art that HAART therapy could be

reinitiated after a virologic relapse from previously discontinued HAART. From the teachings of Ganguly, it would have also been obvious to those in the art to use interferon alpha in addition to the reinitiated HAART. Further, the Reynes abstract provides further grounds for a reasonable expectation of success in using such a combination for the treatment of HIV in that the reference shows that the combination had an effective retroviral activity. Thus, the combined teachings of these references render obvious the presently claimed invention.

20. **(Prior Rejection- Withdrawn)** Claims 7, and 11-17 were rejected under 35 U.S.C. 103(a) as being unpatentable over Gilbert et al., U.S. Patent 6,042,822, in light of the teachings of Testa or Alber as applied to claims 1, 5, and 6 above. These claims describe methods of promoting HIV-1 specific immune responses in a patient by administering to the patient effective doses of pegylated interferon-alpha. As indicated above, Testa and Alber each teach methods of promoting such responses in patients by administering non-pegylated interferon-alpha. In view of the cancellation of the rejected claims, the rejection is withdrawn.

21. **(Prior Rejection-Withdrawn)** Claims 41, 42, 44, and 45-49 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over either Alber or Weiner et al., U.S. Patent 5,780,220, further in view of Gilbert. The claims have been amended to specify that the patients treated by the claimed methods are patients having an HIV-1 infection and who have discontinued HAART and experienced an increase in HIV-RNA plasma levels, and wherein the anti-HIV therapy used in the method with interferon alpha is HAART. In view of these amendments, the rejection is withdrawn.

22. **(Prior Rejection-Maintained)** Claims 1-4, 6, 7-10, 12-24, and 25-40 were rejected under 35 U.S.C. 103(a) as being unpatentable over Gilbert (supra), in view of Vandamme et al. (Antiviral Chemistry and Chemotherapy 9:197-203), and further in view of Kalams et al. (Journal of Virology 73(8): 6721-28), and Alber (supra). Of these claims, claims 25, 27, 28, and 32-36 are still pending in the application. These claims read on methods of treating patients who have ceased HAART, and wherein the patient is thereafter provided with alternating treatments of IFN-alpha and HAART. The Applicant has traversed the rejection as it applies to these claims by arguing that Vandamme teaches that the alternative strategies could be used once the viral load is undetectable, whereas, in the claimed methods, the interferon-alpha is administered after an increase in the HIV-RNA serum levels. The Applicant argues that the reference therefore teaches away from the presently claimed invention. This argument is not found persuasive, and the rejection is therefore maintained against the pending claims.

The Applicant argues that the teachings of Vandamme teach away from the use of interferon alpha once the HIV-RNA serum levels are no longer undetectable. However, Vandamme merely teaches that, one the serum levels are undetectable, it would then be prudent to use other forms of anti-viral treatment. Further, the Applicant has ignored the teachings of the other references identified in the rejection. In particular, the teachings of Gilbert and Alber each illustrate that interferon alpha is effective in the treatment of HIV, and do not limit the compounds use to times wherein the HIV-RNA serum levels are undetectable. Thus, it would have been obvious to those in the art to use the interferon alpha until such time as the doctor felt that re-initiation of HAART was necessary. From the teachings of Gilbert and Alber, there would

have been a reasonable expectation in the art that use of the interferon alpha in the meantime would have provided an effective alternative strategy. Further, due to the teachings of Kalams, Vandamme, and Alber regarding the CTL activities surrounding these alternative strategies, it would have been obvious to those in the art to use these two treatments on an alternative basis. The Applicant's arguments in traversal are therefore not found persuasive, and the rejection is maintained against pending claims 25, 27, 28, and 32-36.

Double Patenting

23. **(Prior Rejection-Withdrawn)** Claims 1-49 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 9, 11-14, 25, 26, 49-57 60-65, and 68-72 of copending Application No. 09/516,673. In view of the terminal disclaimer filed in this application by the Applicant on November 20, 2003 with reference to the copending application, the rejection is withdrawn.

Conclusion

24. No claims are allowed.

25. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner

James C. Housel 2/9/04
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